CSCanada
Advances in Natural Science
Vol. 4, No. 2, 2011, pp. 113-122
DOI:10.3968/j.ans.1715787020110402.558

ISSN 1715-7862 [PRINT]
ISSN 1715-7870 [ONLINE]
www.cscanada.net
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The Actinidic Archaea Related Lemurian Syndrome-Endomyocardial Fibrosis, Chronic Calcific Pancreatitis and Multinodular Goitre-Evolutionary Significance and Evidence for the Lemurian Supercontinent

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Received 17 September 2011; accepted 19 November 2011

Abstract

Background: Endogenous digoxin has been related to the pathogenesis of chronic calcific pancreatitis, endomyocardial fibrosis, multinodular goitre and mucoid angiopathy which are seen in South India, South Africa, Australia and South America. Phytoplasmas, viroids and rutile in beach sands have been related to root wilt disease of coconut seen in the same endemic area. The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism as well as a RNA viroid role in pathogenesis of these endemic diseases was considered. The study aims to link actinidic nanoarchaea to etiology of these diseases and postulates their common geographic epidemiology to the existence of a pre-historic Lemurian supercontinent linking these geographic areas. It also postulates a role for actinidic surfaces in the evolution of life, eukaryote, primates and humans.

Methods: 10 cases each of chronic calcific pancreatitis, endomyocardial fibrosis, multinodular goitre and mucoid angiopathy before starting treatment and 10 age and sex matched healthy controls from general population were chosen for the study. Cholesterol substrate was added to the plasma of the patients and the generation of cytochrome F420, free RNA, free DNA, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and urease were studied. The changes with the addition of antibiotics and rutile to the patient's plasma were also studied. The statistical analysis was done by ANOVA.

Results: The parameters mentioned above were increased the patient's plasma with addition of cholesterol substrate. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels.

Conclusions: An actinide dependent shadow biosphere of archaea and viroids is described in endomyocardial fibrosis, chronic calcific pancreatitis, multinodular goitre and mucoid angiopathy contributing to their pathogenesis. The coexistence of EMF, CCP and MNG in South India, South Africa, Australia and South America is thus an indirect evidence for the existence of the Lemurian supercontinent containing these land masses and rich in actinidic minerals. It also is evidence of abiogenesis on radioactive actinidic beach sands through the process of surface metabolism in the course of evolution. This gives credence to the role of actinidic archaea as the third element that controls life and its role in the evolution of the multicellular eukaryote, primates and humans.

Key words: Archaea; Viroids; Endomyocardial fibrosis; Chronic calcific pancreatitis; Multinodular goitre; Mucoid angiopathy; Lemuria

Ravikumar Kurup, DM, Parameswara Achutha Kurup (2011). The Actinidic Archaea Related Lemurian Syndrome-Endomyocardial Fibrosis, Chronic Calcific Pancreatitis and Multinodular Goitre- Evolutionary Significance and Evidence for the Lemurian Supercontinent. *Advances in Natural Science, 4*(2), 113-122. Available from: URL: http://www.cscanada.net/index.php/css/article/view/j.ans.1715787020110402.558
DOI: http://dx.doi.org/10.3968/j.ans.1715787020110402.558.

INTRODUCTION

Actinidic beach sands have been postulated to play a pivotal role in abiogenesis. Chronic calcific pancreatitis (CCP), endomyocardial fibrosis (EMF), multinodular

goitre (MNG) and mucoid angiopathy along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. The Actinides like rutile producing intracellular magnesium deficiency due to actinide-magnesium exchange sites in the cell membrane has been implicated in the etiology of EMF[1,2,3]. Endogenous digoxin, a steroidal glycoside which functions as a membrane sodium-potassium ATPase inhibitor has also been related to its etiology of EMF, CCP, MNG and mucoid angiopathy[4]. Digoxin produces intracellular magnesium deficiency which results in acidic mucopolysaccharide accumulation of the vascular, cardiac and endocrine tissues contributing to the pathogenesis. Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of root wilt disease of coconut which is co-endemic in Kerala[5,6]. The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered[7,8,9]. The role of RNA viroids in the etiopathogenesis of EMF, CCP, MNG and mucoid angiopathy was also explored. Davies has put forward the concept of a shadow biosphere of organisms with alternate biochemistry present in earth itself[10]. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described[7].

The group of diseases are seen in particular geographic areas of the world near the equator- South India, South America, South Africa and Australia.[1,2,3] These geographic areas are rich in placer deposits containing monazite, illmenite, rutile and thorium. These areas peninsular India, Africa, Australia, south America and Antartica formed part of one single pre-historic continent in Southern ocean and Indian ocean called Lemuria by geologists. The evolution of primates and homo sapiens occurred in the rift valley of Africa part of this pre-historic continent. Metal actinides in beach sands have been postulated to play a role in abiogenesis. Actinide mineral like rutile, monazite and illmenite by surface metabolism would have contributed to abiogenesis. A hypothesis of cholesterol as the primal prebiotic molecule synthesised on actinide surfaces with all other biomolecules arising from it and a self replicating cholesterol lipid organism as the initial life form is presented. Actinide dependent organism would have contributed to primate and human evolution. It is also possible that actinidic organisms would also have contributed to the destruction of the Lemurian supercontinent. This paper postulates that the co-existence of EMF, CCP and MNG in the above mentioned geographic areas points to the possibility of these land masses being joined together has one single land mass- Lemuria.

MATERIALS AND METHODS

Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The following groups were included in the study:- endomyocardial fibrosis, chronic calcific pancreatitis, multinodular goitre and mucoid angiopathy. There were[10] patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[11]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37^{o}C for 1 hour. The following estimations were carried out:- Cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA redutase, digoxin and urease[12,13,14,15]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. The statistical analysis was done by ANOVA.

RESULTS

The parameters checked as indicated above were:- cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and urease. Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-7 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1
Effect of Rutile and Antibiotics on Muramic Acid and Serotonin

	Muramic acid % (Increase without Doxy)		Muramic acid % (Decrease with Doxy)		5 HT % (Increase without Doxy)		5 HT % (Decrease with Doxy)	
Group	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
Muc Angio	24.43	0.81	68.72	2.77	24.32	1.09	65.80	5.14
EMF	22.28	1.52	64.05	2.79	22.82	1.56	64.61	4.95
CCP	23.07	1.46	64.68	3.86	22.89	1.50	64.19	6.51
MNG	23.85	1.69	66.43	3.17	22.72	1.64	63.91	4.93
F value	403.394		680.284		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 2
Effect of Rutile and Antibiotics on Free DNA and RNA

	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy)	
Group	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
Muc Angio	22.27	1.49	63.99	4.03	22.27	1.49	69.25	2.33
EMF	22.29	2.05	58.70	7.34	22.29	2.05	67.03	5.97
CCP	21.19	2.18	61.63	7.68	21.19	2.18	62.99	5.47
MNG	22.93	2.08	63.49	5.01	23.19	1.74	65.68	4.06
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 3
Effect of Rutile and Antibiotics on HMG CoA Reductase and PAH

	HMG CoA R % change (Increase with Rutile)		HMG CoA R % change (Decrease with Doxy)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy)	
Group	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.30	0.20	18.35	0.35	4.45	0.14	18.25	0.72
Muc Angio	24.44	0.90	59.90	4.74	23.90	1.36	63.29	6.86
EMF	22.92	1.48	61.91	7.56	23.73	1.38	65.20	6.20
CCP	23.27	1.96	63.09	9.21	22.85	1.71	66.14	3.58
MNG	23.65	1.88	64.78	6.62	23.79	1.19	64.24	3.96
F value	319.332		199.553		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 4
Effect of Rutile and Antibiotics on Digoxin and Urease

	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Urease % change (Increase with Rutile)		Urease % change (Decrease with Doxy)	
Group	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
Muc Angio	0.53	0.03	0.224	0.041	23.37	1.55	63.99	4.03
EMF	0.51	0.05	0.213	0.033	23.41	1.41	58.70	7.34
CCP	0.47	0.05	0.212	0.028	22.44	2.00	61.63	7.68
MNG	0.51	0.06	0.227	0.040	22.15	1.79	65.49	7.28
F value	135.116		71.706		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 5
Effect of Rutile and Antibiotics on Pyruvate and Hexokinase

	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy)		Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with Doxy)	
Group	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
Muc Angio	22.27	1.49	61.94	5.49	23.67	1.65	69.25	2.33
EMF	22.29	2.05	62.37	5.05	21.66	1.94	67.03	5.97
CCP	21.19	2.18	54.82	8.70	22.27	2.18	62.99	5.47
MNG	19.73	2.27	59.36	7.53	22.51	2.32	62.70	3.24
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 6
Effect of Rutile and Antibiotics on Hydrogen Peroxide and Delta Amino Levulinic Acid

	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy)	
Group	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
Muc Angio	23.64	1.50	60.44	6.83	22.27	1.49	59.90	4.74
EMF	23.29	1.67	60.52	5.38	22.29	2.05	61.91	7.56
CCP	23.38	1.79	57.37	7.45	21.19	2.18	63.09	9.21
MNG	22.00	1.77	61.39	7.47	22.71	1.82	66.13	3.83
F value	380.721		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 7
Effect of Rutile and Antibiotics on Atp Synthase and Cytochrome F 420

	ATP synthase % (Increase with Rutile)		ATP synthase % (Decrease with Doxy)		CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy)	
Group	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.40	0.11	18.78	0.11	4.48	0.15	18.24	0.66
Muc Angio	23.45	1.52	67.05	4.84	23.72	1.76	58.92	5.46
EMF	23.37	1.31	63.97	3.62	22.70	1.87	60.46	8.06
CCP	22.53	1.92	66.31	3.10	21.31	1.37	57.32	8.41
MNG	23.39	1.14	68.11	3.02	22.17	2.01	65.15	6.46
F value	449.503		673.081		306.749		130.054	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Abbreviations
Muc Angio: Mucoid angiopathy
EMF: Endomyocardial fibrosis
CCP: Chronic calcific pancreatitis
MNG: Multinodular goiter

DISCUSSION

There was increase in cytochrome F420 indicating archaeal growth in endomyocardial fibrosis, chronic calcific pancreatitis, multinodular goitre and mucoid angiopathy. The archaea can synthesise and use cholesterol as a carbon and energy source[16,17]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[18]. There was also an increase in archaeal HMG CoA reductase activity indicating increased cholesterol synthesis by the archaeal mevalonate pathway. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis and archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased[8]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[17]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The archaeal aromatization

of cholesterol generating PAH, serotonin and dopamine was also detected[19]. The archaeal glycolytic hexokinase activity and archaeal extracellular ATP synthase activity were increased. There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities[20]. Archaeal pyruvate can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses[21]. The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes[22]. The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites[21,22]. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters[23]. The viroidal complementary DNA can function as jumping genes producing a dynamic genome and changing DNA sequences. The RNA viroids can regulate mrna function by RNA interference[20]. The phenomena of RNA interference can modulate euchromatin/heterochromatin expression. RNA viroidal mRNA interference plays a role in the pathogenesis of endomyocardial fibrosis, chronic calcific pancreatitis, multinodular goitre and mucoid angiopathy. The viroidal RNA modulation of T cell and B cell function by mRNA interference can lead to immune activation. Monocytic infiltration of the vascular wall, cardiac and endocrine tissue can produce reactive connective tissue macromolecular deposition contributing to EMF, CCP, MNG and mucoid angiopathy. The viroidal RNA mediated mRNA interference can also inhibit insulin signalling and secretion leading onto CCP. The viroid RNA can inhibit thyroid hormone secretion and action by mRNA interference leading to increased TSH secretion and multinodular goitre.

The presence of muramic acid, HMG CoA reductase and cholesterol oxidase activity inhibited by antibiotics indicates the presence of bacteria with mevalonate pathway. The bacterial with mevalonate pathway include streptococcus, staphylococcus, actinomycetes, listeria, coxiella and borrelia[24]. The bacteria and archaea with mevalonate pathway and cholesterol catabolism had a evolutionarily advantage and constitutes the isoprenoidal clade organism with the archaea evolving into mevalonate pathway gram positive and gram negative organism through horizontal gene transfer of viroidal and virus genes[25]. The isoprenoidal clade prokaryotes develop into other groups of prokaryotes via viroidal/virus as well as eukaryotic horizontal gene transfer producing bacterial speciation[26]. The RNA viroids and its complementary DNA developed into cholesterol enveloped RNA and DNA viruses like herpes, retrovirus, influenza virus, borna virus, cytomegalo virus and Ebstein Barr virus by recombining with eukaryotic and human genes resulting in viral speciation. Bacterial and viral species are ill defined and fuzzy with all of them forming one common genetic pool with frequent horizontal gene transfer and recombination. Thus the multi and unicellular eukaryote with its genes serves the purpose of prokaryotic and viral speciation. The multicellular eukaryote developed so that their endosymbiotic archaeal colonies could survive and forage better. The multicellular eukaryotes are like bacterial biofilms. The archaea and bacteria with a mevalonate pathway uses the extracellular RNA viroids and DNA viroids for quorum sensing and in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes[27,28]. The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids and DNA viroids for the regulation of muticellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesised PAH and methane leading on to redox stress. Redox stress leads to sodium potassium ATPase inhibition, inward movement of plasma membrane cholesterol, defective SREBP sensing, increased cholesterol synthesis and nanoarchaeal/mevalonate pathway bacterial growth[29]. Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the integration going on as a continuing event. The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality[30]. Thus actinidic nanoarchaea would have contributed to the evolution of the multicellular eukaryote, primates and humans. Changes in the length of noncoding region especially due to integration of viroid complementary DNA and archaea and the resulting jumping genes leads to new DNA sequences possibly contributing to EMF, CCP, MNG and mucoid angiopathy[31]. The integrated viroidal, archaeal and mevalonate pathway bacterial sequences can undergo vertical transmission and can exist as genomic parasites. The genomic integrated archaea, mevalonate pathway bacteria and viroids form a genomic reserve of bacteria and viruses which can recombine with human and eukaryotic genes producing bacterial and viral speciation. Archaea and mevalonate pathway bacteria can lead onto EMF, CCP, MNG and mucoid angiopathy. The persistent symbiosis leads to

reparative connective tissue macromolecular deposition of acidic mucopolysaccharides, glycoproteins, collagen and elastin leading to fibrotic changes in the heart, vessel wall, thyroid and pancreas contributing to EMF, CCP, MNG and mucoid angiopathy[4,32]. The integration of nanoarchaea, mevalonate pathway prokaryotes and viroids in to the eukaryotic and human genome produces a chimera which can multiply producing biofilm like multicellular structures having a mixed archaeal, viroidal, prokaryotic and eukaryotic characters which is a regression from the multicellular eukaryotic tissue. This results in a new metabolic and immune phenotype or microchimeras leading on to human diseases like EMF, CCP, MNG and mucoid angiopathy with a predilection to develop malignancy. Microchimeras can lead to cellular polyploidy important in malignant transformation and induction of carcinoma of thyroid and pancreas. The growth of archaea in the vascular, cardiac and endocrine tissues can result in calcification. The archaea can form calcified nanoarchaeal structures which can exist as colonies in slime. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[33]. The calcified nanoarchaea can contribute to the tissue calcification noted in CCP, MNG and mucoid angiopathy.

Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation and cytokine TNF alpha secretion. The archaeal DXP and mevalonate pathway metabolites can bind γδ TCR and digoxin induced calcium signaling can activate NFKB producing chronic immune activation[4,34]. The archaea and viroid can induce chronic immune activation and generation of superantigens. The archaea and viroid induced chronic immune activation can lead to monocyte infiltration of the vessel wall, cardiac and endocrine tissues leading on to reparative connective tissue macromolecular deposition. Immune activation results in induction of NADPH oxidase which generates hydrogen peroxide. Cholesterol oxidase activity also generates hydrogen peroxide. Hydrogen peroxide can produce tissue injury in MNG, CCP, EMF and mucoid angiopathy contributing to reparative connective tissue macromolecular deposition. Immune activation can also produce insulin resistance. TNF alpha produced by chronic immune activation can modulate the insulin receptor producing insulin resistance[35]. Chronic immune activation and cholesterol oxidase generated hydrogen peroxide can induce neutral sphingomyelinase generating ceramide producing insulin resistance[36]. This can contribute to chronic calcific pancreatitis. Immune activation and NFKB induction can suppress the thyroid hormone receptor resulting in hypothyroidism and increased TSH levels contributing to thyroid gland enlargement and multinodular goitre. Immune activation and NFKB induction can suppress the nuclear receptors LXR, PXR and FXR. FXR suppression can also lead to insulin resistance as well as increased connective tissue MPS deposition in vessel wall, cardiac tissue and endocrine tissue. LXR suppression by NFKB stimulates HMG CoA reductase activity and suppresses cholesterol 7 alpha hydroxylase activity[37]. This stimulates cholesterol synthesis and inhibits its degradation via the bile acid pathway. PXR suppression by NFKB prevents cholesterol detoxification via the bile acid shunt pathway[38]. Thus LXR and PXR suppression by NFKB produces acute cholesterol toxicity. The increased cholesterol in the system leads to still further archaeal multiplication and growth as they depend on cholesterol as a carbon and energy source.

Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[39]. The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics. Mitochondrial dysfunction owing to the Warburg's phenotype can contribute to ineffective glucose utilisation and CCP. The accumulated pyruvate enters the gaba shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis[39]. The increased cholesterol substrate also leads to increased archaeal growth and digoxin synthesis due to metabolic channeling to the mevalonate pathway. The Warburg phenotype leads to increased lipid synthesis and defective beta oxidation of fatty acids. The myocardium depends on fatty acids beta oxidation for energetics. The defective beta oxidation of fatty acids leads to myocardial dysfunction and EMF. The Warburg phenotype leads to upregulated glycolysis and increase in the metabolite fructose 1,6 diphosphate which is channelled to the pentose phosphate pathway. This can generate UDP sugars used for mucopolysaccharide synthesis. This results in acidic MPS deposition in the tissues leading onto EMF, CCP, MNG and mucoid angiopathy. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. Ammonia can stimulate membrane sodium-potassium ATPase, increase ATP utilisation and produce mitochondrial transmembrane potential changes leading to mitochondrial dysfunction. This causes defective glucose utilisation contributing to CCP. Archaeal urease can convert urea to ammonia and thiocyanate. Increase cyanide load in the system can lead to mitochondrial dysfunction[3]. Cyanide related mitochondrial dysfunction can produce EMF, CCP and MNG. It produces defective cardiac function, decreased glucose utilisation and impaired iodide transport into the thyroid follicular cells. The Warburg phenotype can also lead onto malignant transformation. The upregulated glycolysis results in increased mitochondrial PT pore hexokinase and cell proliferation producing carcinoma of

thyroid and pancreas.

Digoxin can produce sodium-potassium ATPase inhibition and inward movement of plasma membrane cholesterol. This produces defective SREBP sensing, increased HMG CoA reductase activity and cholesterol synthesis[29]. The digoxin induced inward movement of plasma membrane cholesterol can alter membrane cholesterol/sphingomyelin ratio producing modified lipid microdomains[40]. The digoxin induced lipid microdomain modulation can regulate the GPCR couple adrenaline, noradrenaline, glucagon and neuropeptide receptors as well as protein tyrosine kinase linked insulin receptor. This can lead onto CCP. The digoxin mediated inhibition of nuclear membrane sodium-potassium ATPase can modulate nuclear membrane lipid microdomains and thyroxine DNA receptor function. This can lead onto hypothyroidism, increased TSH levels and thyroid gland enlargement contributing to MNG. Digoxin can produce intracellular hypercalcemia and hypomagnesemia. This can lead on to vasospasm and thrombosis. Intracellular hypercalcemia can activate the G-protein coupled thrombin receptor and PAF receptor producing thrombosis. Intracellular magnesium deficiency can lead onto increased thrombin and ADP/collagen induced platelet aggregation. This leads onto the thrombotic state in mucoid angiopathy. The decreased intracellular magnesium can produce ATP synthase inhibition and the increased intracellular calcium can produce mitochondrial PT pore dysfunction. Mitochondrial dysfunction can contribute to decreased glucose utilisation in CCP and myocardial dysfunction in EMF. Digoxin can produce sodium-potassium ATPase inhibition and intracellular hypomagnesemia. The increased tissue rutile load can lead to rutile-magnesium exchange leading onto intracellular hypomagnesemia. Hypomagnesemia can lead onto upregulated connective tissue macromolecular synthesis contributing to MNG, CCP, EMF and mucoid angiopathy. Acidic MPS deposition in the vessel wall leads to a hose pipe narrowing of the entire vascular tree leading onto mucoid angiopathy. Acidic MPS, collagen and elastin deposition of the heart leads to EMF. Hyperdigoxinemia is important in the pathogenesis of EMF, CCP, MNG and mucoid angiopathy. Digoxin induced sodium-potassium ATPase inhibition results in an ATP sparing effect[41]. Eighty percent of the ATP generated is used to run the sodium-potassium ATPase pump. The digoxin inhibition of the sodium-potassium ATPase spares this ATP which is then used for lipid and cholesterol synthesis. Fat also fuels insulin resistance by binding to the toll receptor and producing immune activation and immune infiltration of the adipose tissue. Digoxin can also increase lymphocytic intracellular calcium which leads on to induction of NFKB and immune activation[4]. The archaeal cholesterol catabolism can deplete the lymphocytic cell membranes of cholesterol resulting in alteration of lymphocytic cell membrane microdomains related receptors producing immune activation, monocytic infiltration and reparative connective tissue macromolecular deposition.

NMDA can be activated by digoxin induced calcium oscillations, PAH and viroid induced RNA interference4. The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate. Glutamatergic transmission can lead to immune activation. Immune activation can lead to reparative connective tissue macromolecular deposition in EMF, CCP, MNG and mucoid angiopathy. The cholesterol aromatase generated serotonin is well known to produce connective tissue macromolecule especially collagen deposition producing the fibrotic changes in EMF, mucoid angiopathy, MNG and CCP. The archaeal cholesterol aromatase can generate PAH[19]. The PAH can also lead to insulin resistance and CCP. PAH can also inhibit thyroid hormone receptor function contributing to hypothyroidism, increased TSH, thyroid enlargement and MNG. Particulate pollution has been related to vascular thrombosis and can lead to mucoid angiopathy. PAH particles are also known to produce myocardial dysfunction. Thus the actinide, viroid and mevalonate pathway bacteria induced metabolic, genetic, immune and neuronal transmission changes can lead onto endemic EMF, CCP, MNG and mucoid angiopathy. The term archaea and viroid induced endemic cardiovascular and endocrine mucopolysaccharidoses can be used to describe this entity.

The metal actinides provide radiolytic energy, catalysis for oligomer formation and provide a coordinating ion for metalloenzymes all important in abiogenesis[6]. The metal actinide surfaces would by surface metabolism generate acetate which could get converted to acetyl CoA and then to cholesterol which functions as the primal prebiotic molecule self organizing into self replicating supramolecular systems, the lipid organism[42]. Cholesterol by radiolysis by actinides would have formed PAH generating PAH aromatic organism[8]. Cholesterol radiolysis would generate pyruvate which would get converted to amino acids, sugars, nucleotides, porphyrins, fatty acids and TCA acids. Anastase and rutile surfaces can produce polymerization of amino acids, isoprenyl residues, PAH and nucleotides to generate the initial lipid organism, PAH organism, prions and RNA viroids which would have symbiosed to generate the archaeal protocell. The archaea evolved into gram negative and gram positive bacteria with a mevalonate pathway which had a evolutionary advantage and the symbiosis of archaea with gram negative organism generated the eukaryotic cell[43]. The data supports the persistence of an actinide and cholesterol based shadow biosphere which throws light on the actinide based origin of life and cholesterol as the premier prebiotic molecule. The presence of placer deposits and mineral sands containing monazite, illmenite, rutile and thorium in the Lemurian supercontinent would have made it the ideal place for the primitive cell, nanoarchaea, eukaryote, multicellular eukaryote,

primates and humans to evolve. Anthropological studies have provided evidence for the evolution of primates and homosapiens in the rift valley of Kenya part of the prehistoric Lemurian continent.

The archaea can synthesise magnetite by biomineralization. The archaeal cholesterol catabolism can generate PAH. The archaea can exist as nanoarchaea and can have calcified nano forms. The actinidic magnetotactic nanoarchaea and its secreted PAH organisms are extremophiles and survive in the interstellar space and can contribute to the interstellar grains and magnetic fields which play a role in the formation of the galaxies and star systems[44]. The cosmic dust grains occupy the intergalactic space and are thought to be formed of magnetotactic bacteria identified according to their spectral signatures. According to the Hoyle's hypothesis, the cosmic dust magnetotactic bacteria plays a role in the formation of the intergalactic magnetic field. A magnetic field equal in strength to about one millionth part of the magnetic field of earth exists throughout much of our galaxy. The magnetic files can be used to trace the spiral arms of the galaxy following a pattern of field lines that connect young stars and dust in which new stars are formed at a rapid rate. Studies have shown that a fraction of the dust particles have elongated shape similar to bacilli and they are systematically lined up in our galaxy. Moreover the direction of alignment is such that the long axes of the dust tend to be at right angles to the direction of the galactic magnetic field at every point. Magnetotactic bacteria have the property to affect the degree of alignment that is observed. The fact that the magnetotactic bacteria appear to be connected to the magnetic field lines that thread through the spiral arms of the galaxy connecting one region of star formation to another support a role for them in star formation and in the mass distribution and rotation of stars. The nutrient supply for a population of interstellar bacteria comes from mass flows out of supernovas populating the galaxy. Giants arising in the evolution of such stars experience a phenomenon in which material containing nitrogen, carbon monoxide, hydrogen, helium, water and trace elements essential for life flows continuously outward into space. The interstellar bacteria need liquid water. Water exists only as vapour or solid in the interstellar space and only through star formation leading to associated planets and cometary bodies can there be access to liquid water. To control conditions leading to star formation is of paramount importance in cosmic biology. The rate of star formation is controlled by two factors: Too high a rate of star formation produces a destructive effect of UV radiation and destroys cosmic biology. Star formation as stated before produces water crucial for bacterial growth. Cosmic biology of magnetotactic bacteria and star formation are thus closely interlinked. Systems like solar systems do not arise in random condensation of blobs of interstellar gas. Only by a rigorous control of rotation of various parts of the system would galaxies and solar system evolved. The key to maintaining control over rotation seems to lie in the intergalactic magnetic field as indeed the whole phenomena of star formation. The intergalactic magnetic fields owes its origin to the lining up of magnetotactic bacteria and the cosmic biology of interstellar bacteria can prosper only by maintaining a firm grip on the interstellar magnetic field and hence on the rate of star formation and type of star system produced. This points to a cosmic intelligence or brain capable of computation, analysis and exploration of the universe at large- of magnetotactic bacterial networks. The origin of life on earth according to the Hoyle's hypothesis would be by seeding of bacteria from the outer intergalactic space. Comets carrying microorganisms would have interacted with the earth. A thin skin of graphitized material around a single bacteria or clumps of bacteria can shield the interior from destruction by UV light. The sudden surge and diversification of species of plants and animals and their equally sudden extinction has seen from fossil records point to sporadic evolution produced by induction of fresh cometary genes with the arrival of each major new crop of comets[45,46]. The interstellar PAH aromatic organism is formed from nanoarchaeal cholesterol catabolism. The PAH and cholesterol are the interconvertable primal prebiotic molecules. PAH aromatic organism and nanoarchaeal magnetite can have a wave particle existence and bridge the world of bosons and fermions. The nanoarchaea can form biofilms and the PAH aromatic organism can form a molecular quantum computing cloud in the biofilm which forms a interstellar intelligence regulating the formation of star systems and galaxies. The magnetite loaded nanoarchaeal biofilms and PAH aromatic organism quantal computing cloud can bridge the wave particle world functioning as the anthropic observer sensing gravity which orchestrates the reduction of the quantal world of possibilities in to the macroscopic world. The actinide based nanoarchaea can regulate the earth's carbon cycle by methanogenesis, nitrogen cycle by ammonia oxidation and rain formation by contributing the seeding nucleus. The earth's temperature and global warming and cooling are regulated by nanoarchaeal synthesised PAH from cholesterol and methanogenesis. The increased nanoarchaeal growth in ocean beds and soil leads to increased methane production and movement of the earth's crust producing tsunamis and massive earthquake leading to catastrophic mass extinction[47]. This nanoarchaeal growth in the Southern ocean and Indian ocean bed due to global warming induced by civilizational progress and human activity would have led to methane burps in the ocean bed contributing to massive earthquakes leading onto Tsunamis. This would have led to catastrophic destruction of the Lemurian supercontinent. The migration of the Lemurian survivors into the Indian subcontinent Indus valley, the Nile valley and the Mesopotamian valley would have contributed

to the origin of the Harappan, Sumerian and Egyptian civilization which have all evolved during the same period of human history.[48,49] The eternal nanoarchaea survive and start the cycle of evolution once more. The actinide based nanoarchaea regulates the human system and biological universe.

The coexistence of EMF, CCP and MNG in South India, South Africa, Australia and South America is thus an indirect evidence for the existence of the Lemurian supercontinent containing these land masses. The actinidic nanoarcheal growth would have led to methane burps in the ocean bed contributing to earthquakes and Tsunamis producing extinction of the Lemurian supercontinent. It also supports the abiogenesis on radioactive actinidic beach sands through the process of surface metabolism. This gives support to the role of actinidic archaea as the third element that controls life and its role in the evolution of the multicellular eukaryote, primates and humans. Civilization and humans would have evolved in the placer deposits and actinidic sand rich pre-historic Lemurian supercontinent in the Indian and Southern ocean.[48,49]

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